REMARKS

Claims 8-27 are pending. Claims 8-27 stand rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. Claims 8-27 stand rejected under 35. U.S.C. 102(a) and 102(e) as being anticipated by Waer et al., U.S. Patent Publication 2004/0077859 ("Waer et al."). Claims 8-27 also stand rejected under 103(a) as being obvious over Iwagaki et al., *Immunological Investigations*, 24(3): 467-478 (1995) ("Iwagaki") and Brown et al., *J. Am. Chem. Soc.*, 86(9): 4413-4420 (1961) ("Brown").

Claims 8-27 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 31 of U.S. Patent Application No. 10/557,541 ("the '541 application").

35 U.S.C. 112, First Paragraph

Claims 8-27 stand rejected under 35 U.S.C. 112 as failing to comply with the enablement requirement. The Office asserts that claim 8 is enabled for the treatment of the toxic effects of TNF-α, alcohol-induced hepatitis, and cachexia but not for the prophylaxis of these disorders. Claim 8, as presently amended, recites only the treatment of the toxic effects of TNF-α, alcohol-induced hepatitis, and cachexia. This ground for rejection is therefore moot.

35 U.S.C. 102(a) and 102(e)

Claims 8-27 stand rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Waer et al. Applicants respectfully disagree. Claims 8-27, as presently amended, recite methods of treatment for the toxic effects of TNF-α, alcohol-induced hepatitis, and cachexia comprising the administration of pteridine compounds. Applicants note that these disorders are absent from the specification of Waer et al. As a result, Waer et al. cannot teach methods of treatment of these disorders. Applicants further note that alcohol-induced hepatitis, as recited in the instant application, is a disorder distinct from viral hepatitis. Because Waer et al. fails to teach each and every limitation of the claims, this ground for rejection should therefore be withdrawn.

35 U.S.C. 103(a)

Claims 8-27 stand rejected under 35 U.S.C. 103(a) as being obvious over Iwagaki in light of Brown. Claims 8-27 are directed, in part, to a method of treatment of cachexia by administration of the pteridine compounds of the invention. The Office asserts that Iwagaki teaches (citing page 476, Figure 5, and text thereafter):

- an increase in neopterin (NPT) production and presence in tumor cells is indicative of cancer cachexia;
- NPT levels inversely correlate with tryptophan (Trp) levels; and

- increased levels of tryptophan would reflect a decrease in levels of NPT, thereby effectively treating and potentially preventing cachexia.

The Office further asserts that NPT is an obvious variation of the core structure of the instant invention based on the examples of Brown which teach the derivatization of certain pteridine derivatives. As a result, the Office argues that it is *prima facie* obvious to modify the teachings of Iwagaki by using the pteridine compounds of the instant application. Applicants respectfully disagree with this analysis.

Iwagaki shows that increased NPT levels correlate with increased activity by IFN-γ which, in turn, can induce the production of indoleamine 2,3-dioxygenase (IDO; first paragraph on page 473). IDO degrades Trp to kynurenine and therefore decreases Trp levels (see the first paragraph on page 473). Based on the experimental findings, Figure 5 of Iwagaki, as cited by the Office, illustrates a proposed hypothesis of cancer cachexia in which the increased levels of tryptophan—and decreased NPT levels—correlate with a more normal nutritive state. Iwagaki thus proposes that effective therapy may result from maximization of Trp levels and, as a result of the inverse relationship with NPT, minimization of NPT levels (see pages 474-475). As a result, Iwagaki teaches away from the administration of pteridine compounds for the treatment of cachexia, as it does not teach or suggest that NPT could be useful for the treatment of cachexia. Brown cannot remedy the deficiency of Iwagaki because it also fails to teach or suggest the utility of NPT, or any other pteridine compounds, for the treatment of cachexia. Indeed,

there is no evidence of record to indicate that further increasing the amount of pteridine compounds would provide any therapeutic effect on cachexia. For the record, Applicants also disagree that NPT and the compounds described by Brown are obvious variants of the compounds recited in the instant claims and reserve the right to address this argument in the future, if necessary. Because the combined references cannot teach or suggest the claimed invention, they do not support the Office's finding of *prima facie* obviousness, and this ground for rejection should be withdrawn.

Nonstatutory Obviousness-Type Double Patenting

Claims 8-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 31 of the '541 application. Applicants note this claim has been canceled, and the rejection is therefore moot.

With regard to co-pending U.S. Patent Applications Nos. 10/595,126 and 11/402,423, Applicants choose to defer review of these applications until such time as otherwise-allowable subject matter is identified.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including August 12, 2008.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: August 12, 2008

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